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RESIDENTIAL EXPOSURE TO MAGNETIC FIELDS AND ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

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ABSTRACT

Background Previous studies found associations between childhood leukemia and surrogate indicators of exposure to magnetic fields (the power-line classification scheme known as "wire coding"), but not between childhood leukemia and measurements of 60-Hz residential magnetic fields.

Methods We enrolled 638 children with acute lymphoblastic leukemia (ALL) who were under 15 years of age and were registered with the Children's Cancer Group and 620 controls in a study of residential exposure to magnetic fields generated by nearby power lines. In the subjects' current and former homes, data collectors blinded to the subjects' health status measured magnetic fields for 24 hours in each child's bedroom and for 30 seconds in three or four other rooms and outside the front door. A computer algorithm assigned wire-code categories, based on the distance and configuration of nearby power lines, to the subjects' main residences (for 416 case patients and 416 controls) and to those where the family had lived during the mother's pregnancy with the subject (for 230 case patients and 230 controls).

Results The risk of childhood ALL was not linked to summary time-weighted average residential magnetic-field levels, categorized according to a priori criteria. The odds ratio for ALL was 1.24 (95 percent confidence interval, 0.86 to 1.79) at exposures of 0.200 μT or greater as compared with less than 0.065 μT. The risk of ALL was not increased among children whose main residences were in the highest wire-code category (odds ratio as compared with the lowest category, 0.88; 95 percent confidence interval, 0.48 to 1.63). Furthermore, the risk was not significantly associated with either residential magnetic-field levels or the wire codes of the homes mothers resided in when pregnant with the subjects.

Conclusions Our results provide little evidence that living in homes characterized by high measured time-weighted average magnetic-field levels or by the highest wire-code category increases the risk of ALL in children. (N Engl J Med 1997;337:1-7.)

RESULTS of investigations of a possible link between childhood leukemia and residential exposures to magnetic fields at a frequency of 50 to 60 Hz from nearby power lines have been inconsistent.[1-9] In a recent comprehensive report,[10] consistent two- to threefold excesses of leukemia among U.S. children were associated with surrogate indicators of residential magnetic-field exposure,[1,3,5] such as the Wertheimer–Leeper power-line classification scheme,[1,3,11] hereafter designated "wire coding." These surrogate indicators use visual assessments of power lines near homes to estimate magnetic-field measurements within the homes. Wire coding includes characteristics of power lines such as distance from the home and physical configuration. An excess incidence of leukemia in Swedish children was linked to estimated electrical current flow, derived from historical records of power companies and the configuration of high-voltage power lines close to homes where the children lived at the time of diagnosis.[6] However, the risk of childhood leukemia has not been correlated with residential measurements of magnetic fields made shortly after the time of diagnosis.[3-6]

The shortcomings of earlier epidemiologic studies have been extensively reviewed.[10,12-15] Inconsistent

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findings, discrepancies between results based on proxy estimates and those based on direct magnetic-field measurements, and the absence of supportive laboratory evidence or a plausible biologic mechanism of disease causation[10,16] have resulted in uncertainties about the relation, if any, between childhood leukemia and exposure to magnetic fields. Widespread concern and the limitations of previous studies led us to evaluate residential exposure to magnetic fields in a comprehensive case–control study of acute lymphoblastic leukemia (ALL) in childhood, conducted by the Children's Cancer Group.

METHODS

Subjects

The methods of this study are described in detail elsewhere.[17] Briefly, a group of the 1914 children with ALL and the 1987 controls participating in a nationwide telephone-interview study conducted by the Children's Cancer Group was eligible for the assessment of residential exposure to magnetic fields. Eligible case children received a diagnosis of ALL before the age of 15 years, between 1989 and 1994, and were registered with the Children's Cancer Group. Eligible controls were selected by random-digit telephone dialing[18] and were individually matched to the children with ALL according to the first eight digits of the telephone number, age, and race. Eligibility for the assessment of magnetic-field exposure was restricted to the 851 case patients and the 825 controls who participated in the initial telephone interview (representing 96 percent and 75 percent, respectively, of those who were eligible) and who resided in one of nine states (Illinois, Indiana, Iowa, Michigan, Minnesota, New Jersey, Ohio, Pennsylvania, and Wisconsin) on the reference date, defined as the date of diagnosis of ALL for each case patient. The same date was assigned to the case patient's matched control for the purpose of determining which children's residences would have magnetic-field assessments. Mothers of 98 percent of the children with ALL (832 case patients) and 97 percent of the controls (n = 801) who responded to the telephone interview also provided lifetime residential histories for the subjects. Because we did not evaluate 65 of these case patients and 76 of the controls further, once the sample-size goals had been achieved, 767 case patients and 725 controls were eligible for measurements of residential magnetic fields.[17]

For each child under the age of five years, we attempted to measure magnetic fields in all the homes the subject had lived in for at least six months and required that at least 70 percent of the child's life have been spent in the measured homes. For each child over the age of five, we measured one or two homes, provided that the child had lived in them for at least 70 percent of the five years immediately preceding the reference date. We chose the five-year reference period closest to the date of diagnosis because of hypothesized cancer-promoter effects, since no evidence exists that the low strength of residential magnetic fields can induce genotoxic effects.[10,16]

Overall, 78 percent of the eligible patients participated (83 percent participation among the 767 case patients eligible for residential measurements times 98 percent participation in the lifetime residential history times 96 percent participation in the initial telephone interview), as did 63 percent of the controls (86 percent participation among the 725 eligible controls times 97 percent and 75 percent, respectively), resulting in a final study population of 638 case patients and 620 controls. Reasons for nonparticipation included refusal by the child's parents, inability to locate the child or too many changes of residence, lack of approval by the hospital institutional review board for the magnetic-field measurements, and refusal by the child's physician (this was a factor only for the children with cancer). Some subjects could not be included because the current occupants of subjects' former homes denied permission for the magnetic-field measurements.

We ascertained the residential wire-code category for a subgroup of the pairs of children with ALL and their controls who were eligible for magnetic-field measurements. We restricted assessment of wire codes to pairs in which both the case patient and the matched control had "residential stability" — that is, both paired members had lived in one home for at least 70 percent of the reference period (this residence is hereafter designated the "main residence"). Among the 428 such residentially stable pairs identified, 12 pairs were excluded because the technician could not locate the home or accurately diagram nearby power lines at one of the residences. Technicians assessed most homes eligible for wire-code classification even if they could not obtain permission to measure magnetic fields, since access to the residence or the surrounding property was not necessary for wire coding. To evaluate the risk of ALL associated with the subject's residential wire code during the mother's pregnancy with the subject, technicians evaluated residences in which the subject's family had resided for at least five months during the index pregnancy ("residence during pregnancy") for all subjects under the age of three years (151 matched case–control pairs) and for those whose homes were assessed as part of the wire coding of the main residence, for a total of 230 case–control pairs.

Measurement Protocol

Magnetic-Field Measurements

Technicians blinded to the subjects' case or control status used an Emdex-C meter (Electric Field Measurements, West Stockbridge, Mass.), which measures extremely-low-frequency magnetic fields (40 to 300 Hz, a range that includes 50-Hz and 60-Hz levels, frequencies evaluated in prior epidemiologic studies) with a three-axis induction-coil sensor.[17] Derived from two personal-exposure studies,[19,20] the standardized measurement protocol included a 24-hour measurement in the child's bedroom (with the meter placed under or adjacent to the bed); 30-second measurements in the center of the child's bedroom, the family room, the kitchen, and the room in which the mother slept during the index pregnancy; and a 30-second outdoor measurement made within 0.9 m (3 ft) of the front door.[17]

Wire Coding

Technicians (who were unaware of whether a case patient or a control currently or formerly lived in each residence evaluated) drew diagrams and recorded systematically the distance from the home of any overhead power lines within 46 m (150 ft) of the residence, including transmission lines, thick and thin three-phase primary-distribution lines (which carry electric power from substations to surrounding neighborhoods), any open (with separated wires) or spun (with wires bound together) secondary distribution lines, and first-span secondary distribution lines.[17] On the basis of the diagrams, a computer algorithm assigned a wire code to each residence according to the five-category Wertheimer–Leeper classification[1,3,11] and the modified three-category Kaune–Savitz scheme.[21] As in earlier studies,[3,5] we found that measured magnetic-field levels (i.e., the arithmetic means of 24-hour measurements from 858 residences) rose with increasing Wertheimer–Leeper[1,3,11] and Kaune–Savitz[21] wire-code categories (unpublished data).

Statistical Analysis

Magnetic-Field Measurements

For each eligible residence, a summary magnetic-field level was calculated from a weighted average of the room measurements. The weights were derived from the personal-exposure study and based on the estimated time spent by children according to age.[17,19,20] If measurements were not obtained in all rooms, then the weighted average was based on a standardized hierarchy of measurements.[17] The primary measure of exposure for each subject was an average

of the summary level for all the eligible measured homes, weighted according to the duration of residence. We used odds ratios and 95 percent confidence intervals to estimate the risk of ALL.[22] Before undertaking any case–control comparisons, we identified four exposure categories for residential magnetic-field levels (<0.065 μT [the reference group], 0.065 to 0.099 μT, 0.100 to 0.199 μT, and ≥ 0.200 μT), based on the distribution of measurements in the control homes. These categories were similar to those used in earlier investigations.[3,5,6] We calculated results using unmatched analysis as well as analysis of matched case–control pairs.[22]

We used stratified and logistic-regression analyses to explore the effects of age at the reference date, sex, race (though the very small number of nonwhites limited this evaluation), socioeconomic status (indicated by family income, the mother's and father's educational level and occupation, home ownership, and family size), temporal factors (year, season, and time of day when the measurements were made), demographic characteristics (degree of urbanization and type of residence), and dose–response relations using continuous measurements.[22] We also evaluated birth order, birth weight, the mother's age at the child's delivery, and medical x-ray studies during pregnancy as potential confounding factors. We excluded nine case patients and one control who had Down's syndrome, since this disorder has been linked to 10- to-40-fold increases in the risk of acute leukemia.[23] We included 629 case patients and 619 controls in the final unmatched analysis, and 463 case–control pairs in the matched analysis.

Wire Coding

Because the relation between power-line configurations and magnetic-field strength may vary geographically,[5,24] we retained the matched design of the initial nationwide phase of the study for the wire coding of the main residence. The Wertheimer–Leeper wire-code categories used in the analysis include underground (buried) power lines plus very-low-current configuration (the reference group), ordinary low-current configuration, ordinary high-current configuration, and very-high-current configuration.[1,3,11] The modified Kaune–Savitz wire-code categories were as follows: low (the reference group), medium, and high.[21] We used matched-pairs analysis to evaluate the risk of ALL in relation to the wire-code category of the main residence (including 408 case–control pairs, after the exclusion of subjects with Down's syndrome) and the residence during pregnancy (a total of 225 pairs, including 149 pairs of subjects under the age of three, after the exclusion of subjects with Down's syndrome); conditional logistic regression was used to control for socioeconomic and demographic factors and other potential confounders.[22]

RESULTS

Characteristics of the Subjects

The controls were similar to the case patients (Table 1), except for their higher total family income ($P<0.001$). ALL was not associated with the mother's age at delivery of the subject, the number of children in the family, the birth order of the subject (data not shown), the type of residence, the degree of urbanization, home ownership, or the interval between the reference date and the date of the measurements (data not shown). All estimates of risk have been adjusted for the age of the subject at the reference date, the subject's sex, the mother's educational level, and family income.

Summary Measures of Residential Magnetic-Field Exposures

Risk estimates based on the summary residential magnetic-field exposures for a priori measurement categories did not differ significantly from unity either for all the subjects (629 case patients and 619 controls) or for the 463 matched pairs (Table 2), nor did risk increase significantly with increasing summary magnetic-field levels (P for trend = 0.22 for the unmatched analyses and 0.12 for the matched analyses). Risk was higher with estimated summary exposures of 0.300 μT or more (odds ratio, 1.72; 95 percent confidence interval, 1.03 to 2.86; 45 case patients and 28 controls); however, risk did not increase significantly with increasing exposure when exposure was evaluated as a continuous variable (P for trend = 0.15 for the unmatched analysis and 0.09 for the matched analysis).

When the analysis was restricted to subjects who lived in a single home during the study period or to those who lived for the entire reference period in homes for which we obtained 24-hour bedroom measurements, the risks differed little from those shown in Table 2 (data not shown). The results were also virtually unchanged if a partial time-weighted average bedroom measurement for less than 24 hours (i.e., 4 p.m. to 6 a.m. or 10 p.m. to 6 a.m.) was substituted for the full 24-hour average to reflect more accurately the specific period of time subjects spent in their bedrooms. Also, risk estimates were similar after adjustment for differences between case patients and controls in the calendar year, season, or time of day of the measurements. We found no consistent pattern in the relation of summary residential magnetic-field levels to the risk of ALL according to family income, parental educational level or occupation, birth order, or other socioeconomic or residential characteristics.

Main-Residence Wire-Code Patterns

For the main residence, we found no association between the risk of ALL and residence in a home classified in the highest wire-code category according to either wire-code classification (Table 3). There were no positive or statistically significant dose–response trends, and results were not materially changed when adjusted for potentially confounding variables.

Magnetic-Field Levels and Wire Codes of Residences during Pregnancy

As regards the homes resided in during pregnancy by the mothers of 257 case patients and 239 controls, the odds ratio for ALL was 0.75 (95 percent confidence interval, 0.45 to 1.24) for a magnetic-field level of 0.065 to 0.099 μT, as compared with the reference category (<0.065 μT); 1.32 (95 percent confidence interval, 0.81 to 2.15) for a level of 0.100 to 0.199 μT; and 1.24 (95 percent confidence interval, 0.69 to 2.23) for a level of 0.200 μT or higher (P for trend = 0.25). Among the 225 matched pairs whose mothers' residences during pregnancy were wire-coded, the odds ratios for ALL were 1.20 (95 percent

TABLE 1. CHARACTERISTICS OF 629 CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (CASE PATIENTS) AND 619 CONTROLS WITH MEASUREMENTS OF 60-HZ RESIDENTIAL MAGNETIC-FIELD LEVELS AND 408 MATCHED CASE–CONTROL PAIRS OF CHILDREN WITH STABLE RESIDENCES AND WIRE-CODING DATA.

CHARACTERISTIC	MAGNETIC-FIELD MEASUREMENTS*		WIRE CODING†	
	CASE PATIENTS (N=629)	CONTROLS (N=619)	CASE PATIENTS (N=408)	CONTROLS (N=408)
	number (percent)			
Age at diagnosis or reference date (yr)‡				
<2	65 (10.3)	81 (13.1)	52 (12.7)	68 (16.7)
2–4	304 (48.3)	273 (44.1)	184 (45.1)	165 (40.4)
5–9	169 (26.9)	182 (29.4)	110 (27.0)	116 (28.4)
≥10	91 (14.5)	83 (13.4)	62 (15.2)	59 (14.5)
Sex				
Male	329 (52.3)	323 (52.2)	204 (50.0)	218 (53.4)
Female	300 (47.7)	296 (47.8)	204 (50.0)	190 (46.6)
Mother's education				
<12 yr	43 (6.8)	23 (3.7)	32 (7.8)	16 (3.9)
High-school graduate	204 (32.4)	218 (35.2)	132 (32.4)	164 (40.2)
Some college or post–high-school education	215 (34.2)	197 (31.8)	133 (32.6)	112 (27.5)
≥College graduate	167 (26.6)	181 (29.2)	111 (27.2)	116 (28.4)
Annual family income ($)				
<20,000	96 (15.4)	71 (11.5)	63 (15.6)	42 (10.4)
20,000–29,999	117 (18.8)	83 (13.5)	65 (16.0)	51 (12.6)
30,000–39,999	141 (22.6)	105 (17.1)	90 (22.2)	75 (18.5)
40,000–49,999	102 (16.3)	111 (18.0)	62 (15.3)	75 (18.5)
≥50,000	168 (26.9)	245 (39.8)	125 (30.9)	162 (40.0)
Mother's age at birth of subject (yr)				
<25	178 (28.3)	154 (24.9)	106 (26.0)	102 (25.0)
25–29	251 (39.9)	257 (41.5)	162 (39.7)	165 (40.4)
≥30	200 (31.8)	208 (33.6)	140 (34.3)	141 (34.6)
No. of children in family				
1	90 (14.3)	67 (10.8)	56 (13.7)	41 (10.0)
2	280 (44.5)	265 (42.8)	190 (46.6)	184 (45.1)
≥3	259 (41.2)	287 (46.4)	162 (39.7)	183 (44.9)
Type of residence				
Single-family home	509 (83.2)	485 (81.8)	326 (83.2)	319 (82.2)
Apartment	24 (3.9)	25 (4.2)	17 (4.3)	16 (4.1)
Other	79 (12.9)	83 (14.0)	49 (12.5)	53 (13.7)
Home-ownership status				
Owned home	486 (80.2)	499 (84.6)	325 (83.5)	335 (86.8)
Rented home	101 (16.7)	77 (13.0)	58 (14.9)	45 (11.7)
Other	19 (3.1)	14 (2.4)	6 (1.5)	6 (1.6)
Degree of urbanization				
Urban	152 (24.2)	126 (20.4)	117 (28.7)	89 (21.9)
Suburban	278 (44.2)	289 (46.8)	161 (39.5)	192 (47.2)
Rural	199 (31.6)	203 (32.8)	130 (31.9)	126 (31.0)

*Data were missing on income for 5 case patients and 4 controls, on type of residence for 17 case patients and 26 controls, on home ownership for 23 case patients and 29 controls, and on degree of urbanization for 1 control. Percentages are of subjects with data available. See the text for details of magnetic-field measurements.

†Data were missing on income for 3 case patients and 3 controls, on type of residence for 16 case patients and 20 controls, on home ownership for 19 case patients and 22 controls, and on degree of urbanization for 1 control. Percentages are of subjects with data available. See the text for details of wire coding.

‡The reference date for each control was defined as the date of diagnosis in the corresponding matched case patient.

confidence interval, 0.74 to 1.95) for the Wertheimer–Leeper code-configuration category of "ordinary low"; 1.07 (95 percent confidence interval, 0.61 to 1.86) for "ordinary high"; and 1.49 (95 percent confidence interval, 0.66 to 3.37) for "very high," as compared with the reference category of "underground plus very low" (P for trend=0.07). For children under the age of three whose mothers' homes during pregnancy were wire-coded (149 matched pairs), the odds ratios were not significantly elevated and the risks did not increase significantly with higher wire-code categories (P for trend=0.19).

TABLE 2. RISK OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA ACCORDING TO TIME-WEIGHTED AVERAGE SUMMARY LEVELS OF 60-HZ RESIDENTIAL MAGNETIC FIELDS IN THE UNMATCHED AND MATCHED ANALYSIS.*

MAGNETIC-FIELD LEVEL (μT)	UNMATCHED ANALYSIS†			MATCHED ANALYSIS‡		
	NO. OF CASE PATIENTS	NO. OF CONTROLS	OR (95% CI)§¶	NO. OF CASE PATIENTS	NO. OF CONTROLS	OR (95% CI)§‖
<0.065	267	285	1.00	206	215	1.00
0.065–0.099	123	117	1.10 (0.81–1.50)	92	98	0.96 (0.65–1.40)
0.100–0.199	151	143	1.10 (0.83–1.48)	107	106	1.15 (0.79–1.65)
≥0.200	83**	70**	1.24 (0.86–1.79)††	58**	44**	1.53 (0.91–2.56)††
0.200–0.299	38	42	0.92 (0.57–1.48)	29	26	1.31 (0.68–2.51)
0.300–0.399	22	17	1.39 (0.72–2.72)	14	11	1.46 (0.61–3.50)
0.400–0.499	14	5	3.28 (1.15–9.39)	10	2	6.41 (1.30–31.73)
≥0.500	9	6	1.41 (0.49–4.09)	5	5	1.01 (0.26–3.99)

*The analysis used a measure for each subject that was based on the time-weighted average summary values for each eligible home (including measurements in the child's bedroom, family room, and kitchen or outside the front door, weighted according to the age of subject); these values were weighted according to the number of years the subject spent living in each residence.[16,19,20]

†Five case patients and four controls for whom information on confounders was missing are excluded.

‡The controls were matched to the case patients according to age at the reference date, race, and telephone number (first eight digits).

§OR denotes odds ratio, and CI confidence interval.

¶Odds ratios have been adjusted for age at the reference date, sex, mother's educational level, and family income.

‖Odds ratios have been adjusted for sex, mother's educational level, and family income.

**The numbers of case patients and controls are based on four exposure categories.

††The risk estimates are based on four exposure categories selected a priori.

DISCUSSION

We found no significant excess risk of childhood ALL associated with time-weighted average summary residential magnetic-field levels of 0.200 μT or greater, nor did we observe any significant dose–response trends. There was a tendency for the risk to be higher among subjects with summary exposure levels of 0.300 μT or more, but the number of children with such high levels was small. The risk of childhood ALL was not associated with high wire codes for either the subject's main residence or the mother's residence during pregnancy. Adjustment for socioeconomic, demographic, or other potentially confounding variables had little effect on the risk.

In contrast to three earlier U.S. studies,[1,3,5] we found no association between the highest wire-code category and an elevated risk of childhood ALL. Our data demonstrated a significant correlation between measured magnetic fields and wire codes (unpublished data), as was found in previous studies.[24-26] The lack of association between childhood ALL and wire-code categories is particularly noteworthy since public concern[10] has been driven primarily by the excess risks linked with surrogate or historical estimates of residential magnetic-field exposure.[1,3,5,6]

TABLE 3. RISK OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA AMONG 408 MATCHED PAIRS OF CHILDREN WITH STABLE RESIDENCES, ACCORDING TO THE WERTHEIMER–LEEPER AND MODIFIED KAUNE–SAVITZ WIRE-CODE CLASSIFICATIONS OF THE MAIN RESIDENCE.*

WIRE-CODE CATEGORY†	NO. OF CASE PATIENTS	NO. OF CONTROLS	OR (95% CI)‡
Wertheimer–Leeper			
UG+VLCC	175	175	1.00
OLCC	116	114	1.07 (0.74–1.54)
OHCC	87	87	0.99 (0.67–1.48)
VHCC	24	26	0.88 (0.48–1.63)
Kaune–Savitz			
LWC	237	249	1.00
MWC	114	105	1.22 (0.85–1.75)
HWC	51	48	1.04 (0.65–1.66)

*Because of missing data for some variables, the numbers of subjects do not total 408 in each group.

†UG denotes underground or buried power lines, VLCC very-low-current configuration, OLCC ordinary low-current configuration, OHCC ordinary high-current configuration, VHCC very-high-current configuration, LWC low wire code, MWC medium wire code, and HWC high wire code.

‡OR denotes odds ratio, and CI confidence interval. These odds ratios have been adjusted for sex, mother's educational level, and family income.

The results of our measurements of magnetic-field levels, like those of four earlier investigations,[3-6] also show no significant increase in the risk of ALL among children whose residences had measured magnetic-field levels of 0.200 μT or higher, based on a priori categories. The small increase in risk at estimated exposures of 0.300 μT or more derived from a significant excess incidence of ALL at the intermediate level of 0.400 to 0.499 μT, but the odds ratios were close to unity for estimated exposure levels of 0.500 μT or greater, and the P value for trend was not significant. We cannot exclude the possibility of a small increase in risk among children in homes with very high magnetic-field levels, as suggested in studies using historical estimates of residential magnetic-field exposure.[4,6,7]

We designed our investigation to address the limitations of earlier studies, particularly the lengthy intervals (typically years or decades) between the diagnosis of ALL and measurements of magnetic fields. In our study magnetic fields were usually measured within 24 months after the date of diagnosis in the children with ALL.[17] Previous studies also included fewer cases of childhood leukemia, measured fields during a smaller proportion of the reference period or lacked a standardized reference interval for the evaluation of magnetic fields, and evaluated fewer potential confounding variables. Some of the earlier studies selected controls who moved less frequently than the case patients or failed to blind data collectors to the case or control status of the subjects living in each residence evaluated.[10,12-15] We measured residential magnetic-field levels for nearly four times the numbers of case patients and controls in the largest previous investigation.[5] An important strength of our study was that magnetic-field measurements covered more than 95 percent of the reference period for 77 percent of subjects and more than 90 percent of the reference period for 83 percent of subjects.[17]

We made a major effort to achieve a high rate of participation in the study, despite the substantial burden for families (an average of three hours for interviews and measurements). Overall, 78 percent of eligible case patients and 63 percent of eligible controls participated. Many of the reasons for not participating were unrelated to refusal by the subjects or their parents; they included refusals of permission for testing by current occupants of former residences or the failure of subjects to meet eligibility requirements (such as residential stability).

To address concern about possible response bias,[27-29] we instructed the technicians to diagram the homes of 119 children who were identified during random-digit dialing as potential controls but whose parents declined permission for participation; we found that the proportion of these homes assigned by the computer algorithm to the highest wire-code category was similar to that among the subjects in our study.[17] Moreover, the technicians diagrammed virtually all eligible residences of subjects whose families refused permission for magnetic-field measurements, since neither residential nor property access was necessary for assigning wire codes to residences. Residential mobility was similar for case patients and controls in this study, in contrast to an earlier investigation,[3] which has been criticized because the case patients changed residences considerably more often than the controls.[10,12-15] Additional strengths of our investigation included the collection of the exposure data on a blinded basis; the personal-exposure studies to develop[19] and evaluate[20] the measurement protocol; the routine calibration of all magnetic-field (Emdex) meters; the lengthy initial training, retraining, and site visits of measurement staff; the independent rediagramming of a substantial proportion of residences, which showed good concordance of assigned wire codes (unpublished data); and the regular review of all measurements, with detailed investigation of potential errors.[17]

A limitation of our investigation and all previous studies is the absence of measurements for individual residences in the years preceding the diagnosis of cancer. It is not known how well a single 24-hour measurement characterizes contemporary exposure, much less magnetic-field exposure years earlier. Very limited data suggest a moderate correlation between repeated spot measurements taken in the same residential location several years after the initial measurements.[30] To examine the reproducibility and seasonal variation of magnetic-field measurements, we initiated a detailed longitudinal study of 50 homes in Detroit and Minneapolis. The preliminary results suggest good reproducibility and relatively little seasonal variation over a one-year period (Banks R, et al.: unpublished data). Repeated measurements in a large sample of homes over a longer period would help to resolve this issue. The selection of controls by random-digit dialing has known weaknesses,[27] but the use of alternative control groups was not feasible.[17] The only major difference between the case patients and the controls — a higher family income among controls — was probably due to the use of controls obtained by random-digit dialing,[27] but this difference did not confound the relation between magnetic-field exposure and childhood ALL.

In summary, our comprehensive case–control investigation did not find significantly increased risks of ALL associated with time-weighted average summary residential magnetic-field measurements or with residence in homes characterized by a high wire-code category during the five years immediately preceding the diagnosis of ALL or during the index pregnancy. The finding of a tendency for risk to be higher at measured magnetic-field levels of 0.300 μT or greater was based on small numbers and was

not characterized by a consistent pattern or a significant trend. Our results provide little support for the hypothesis that living in homes with high time-weighted average magnetic-field levels or in homes close to electrical transmission or distribution lines is related to the risk of childhood ALL.

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APPENDIX

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